IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Rong Wen, et al.
App. No	:	10/665,203
Filed	:	September 18, 2003
For	:	METHOD OF INHIBITING CHOROIDAL NEOVASCULARIZATION
Examiner	:	Zohreh A. Fay
Art Unit	:	1612
Conf #	:	5747

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DECLARATION OF DAVID A. WEBER PURSUANT TO 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, David A. Weber, under penalty of perjury, declare as follows:

1. I hold a Ph.D. in medical microbiology from Creighton University. As shown in my *curriculum vitae* (attached hereto as Exhibit A) I have broad experience across pharmaceutical, medical device and consumer products. For almost ten years now, I have been employed in the development and commercialization of compounds for ophthalmic use.

2. I am currently employed as the President and Chief Executive Officer of MacuSight, Inc. ("MacuSight") of Union City, California.

3. MacuSight is the sole licensee of the above referenced patent application. As President and Chief Executive Officer of MacuSight I receive remuneration from MacuSight and therefore have an interest in the issuance of the above referenced patent application.

4. I have read and am familiar with the above referenced patent application and the currently pending claims. In addition, I have read the Office Action dated November 18, 2009, and understand that the Office has rejected Claims 30-34, 37-39, 41-48, 50-56, and 63-74 under 35 U.S.C. § 103(a) as allegedly unpatentable over Mollison (US 6,015,815) in view of Kulkarni (US 5,387,589) and Hu et al. (US 5,800,807). The Examiner states that "Hu et al. teach the use of propylene glycol as a safe delivery vehicle for ophthalmic drugs. The above reference makes clear that propylene glycol has been safely and routinely used in ophthalmic compositions" (Office Action, page 2).

5. Prior to development of the inventions of the present application, I like others of skill in the art would have been disinclined from utilizing a hygroscopic composition (e.g., a composition comprising a hydrophobic therapeutic agent and polyethylene glycol) for ophthalmic administration by injection. In particular, intravitreal injection of a polyethylene glycol (PEG)-containing composition was expected to pull water into the eye ball leading to a deleterious increase in intraocular pressure and dessication of retinal tissues. On the other hand, subconjunctival injection of a PEG-containing composition was expected to pull water out of the eye ball leading to a deleterious decrease in intraocular pressure, and swelling. Both scenarios are cause for concern over whether such compositions would temporarily disrupt vision at best, or at worst cause permanent damage to tissues of the eye.

6. Additionally, the ophthalmic compositions currently administered by intravitreal injection (both on and off-label) to treat retinal diseases are all aqueous formulations. In particular, triamcinoline acetonide (KENALOG-40 marketed by Bristol-Myers Squibb), pegaptanib sodium (MACUGEN, marketed by Eyetech-OSI), bevacizumab (AVASTIN, marketed by Genentech) and ranibizumab (LUCENTIS marketed by Genentech) are aqueous formulations or are reconstituted as such prior to ophthalmic administration by injection. Similarly, compositions comprising non-steroidal anti-inflammatory agents, steroids or antibiotics, which are administered off-label by subconjunctival injection, are also aqueous formulations.

7. Finally, since formulations comprising a therapeutic agent and PEG have a greater viscosity than aqueous solutions, administration of the former by injection was expected to require the use of a larger gauge syringe needle. Use of a larger gauge syringe needle is not desirable for ophthalmic administration by injection, since a larger needle is more likely to result

in coring of ocular membranes resulting in a reflux of the formulation and vitreous leakage from the injection site in the eye by virtue of the positive pressure of the eye. Accordingly, use of a very large gauge syringe needle necessitates suturing the eye, and increases the risk of infection as compared to the use of a smaller gauge syringe needle.

8. In summary, prior to development of the inventions of the present application, a viscous, hygroscopic composition such as a formulation comprising rapamycin and PEG was not utilized due to significant safety concerns, as well as an absence of clinical precedence. For the reasons discussed above, as well as the fact that polyethylene glycol is a known eye irritant requiring warning of such on PEG material safety data sheets, PEG was not an accepted excipient for inclusion in injectable ophthalmic formulations.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Dated: May 12, 2010 By _____

David A. Weber, Ph.D.,

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